AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for constitutive and/or inducible gene knock down in a **non-human** vertebrate, or in a tissue culture or cells of a cell culture derived from a **non-human** vertebrate, which comprises stably integrating an expression vector comprising a short hairpin RNA (shRNA) construct under control of a ubiquitous promoter into **a polymerase II dependent locus of** the genome of the **non-human** vertebrate, of the tissue culture or of the cells of the cell culture.

2. (Currently Amended) The method of claim 1, wherein the expression vector ~~is suitable for stabile integration~~ **stably integrates** into the genome of a **non-human** vertebrate~~, or into the genome of the tissue culture or of cells of the cell culture~~.

3. (Currently Amended) The method of claim 1, wherein the expression vector contains homologous sequences ~~suitable for integration at a defined genomic locus~~ **which integrate** through homologous recombination **at a polymerase II dependent locus** in the genome of the vertebrate, in the genome of the tissue culture or in the genome of the cells of the cell culture including embryonic cells.

4. (Canceled)

5. (Currently Amended) The method of claim 4 **1**, wherein the polymerase II dependent locus is selected from the group consisting of a Rosa26, collagen, RNA polymerase,

actin and HPRT locus.

6. (Currently Amended) The method of claim 1, wherein the expression vector further contains functional sequences selected from the group consisting of splice acceptor sequences, polyadenylation sites, **and** selectable marker sequences~~, etc~~.

7. (Original) The method of claim 1, wherein the ubiquitous promoter is selected from the group consisting of polymerase I, II and III dependent promoters.

8. (Original) The method of claim 7, wherein the ubiquitous promoter is a polymerase II or III dependent promoter.

9. (Original) The method of claim 7, wherein the ubiquitous promoter is selected from the group consisting of a CMV promoter, a CAGGS promoter, a snRNA promoter such as U6, a RNAse P RNA promoter such as H1, a tRNA promoter, a 7SL RNA promoter, **and** a 5 S rRNA promoter~~, etc~~.

10. (Original) The method of claim 1, wherein the ubiquitous promoter is a constitutive promoter.

11. (Original) The method of claim 1, wherein the ubiquitous promoter is an inducible promoter.

12. (Original) The method of claim 11, wherein the inducible promoter is a promoter containing a operator sequence selected from the group consisting of tet, Gal4, **and** lac~~, etc~~.

13. (Currently Amended) The method of claim 1, wherein said ~~vertebrate is a~~ non-

human vertebrate **is a mouse or fish**.

14. (Currently Amended) The method of claim 13, wherein said **non-human** vertebrate is a mouse ~~or fish~~.

15. (Currently Amended) The method of claim 1, wherein the expression vector is a Pol III dependent promoter driven shRNA construct ~~suitable~~ to be integrated into a ubiquitously active Pol III dependent locus.

16. (Original) The method of claim 15, wherein the promoter is a constitutive H1 or U6 promoter.

17. (Original) The method of claim 15, wherein the promoter is an inducible U6 or H1 promoter.

18. (Currently Amended) The method of claim 1, wherein the expression vector is a Pol II dependent promoter driven shRNA construct ~~suitable~~ to be integrated into a ubiquitously active Pol II dependent locus.

19. (Original) The method of claim 18, wherein the promoter is an inducible CMV promoter.

20. (Original) The method fo claim 1, wherein the shRNA comprises at least one DNA segment

A-B-C

wherein

A is a 15 to 35 bp DNA sequence with at least 95% complementarily to the gene to be knocked down;

B is a spacer DNA sequence having 5 to 9 bp forming the loop of the expressed RNA hair pin molecule, and

C is a 15 to 35 bp DNA sequence with at least 85% complementarily to the sequence A.

21. (Original) The method of claim 20, wherein A is a 19 to 29 bp DNA sequence.

22. (Original) The method of claim 20, wherein the DNA sequence A has 100% complementarily to the gene to be knocked down.

23. (Original) The method of claim 20, wherein C is a 19 to 29 bp DNA sequence.

24. (Original) The method of claim 1, wherein the shRNA comprises a stop and or polyadenylation sequence.

25. (Canceled)

26. (Currently Amended) The method of claim 1, wherein the method for constitutive and/or inducible gene knock down in a **non-human** vertebrate comprises integrating the expression vector into ES cells of the **non-human** vertebrate.

27. (Currently Amended) A **non-human** vertebrate, or tissue or cell culture derived from a **non-human** vertebrate having stably integrated~~, preferably~~ at a polymerase II dependent locus of the **non-human** vertebrate, tissue culture or cells of the cell culture, an expression vector comprising a short hairpin RNA (shRNA) construct under control of a ubiquitous

promoter.

28. (Canceled)

29. (Currently Amended) The **non-human** vertebrate ~~tissue or cell culture~~ of claim 27, which is or is derived from a mouse or fish.

30. (Currently Amended) An expression vector comprising a short hairpin RNA (shRNA) construct under control of a ubiquitous promoter **and homologous sequences which integrate at a polymerase II dependent locus.**